Know Your Poison - Toxidromes …..

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ABSTRACT

The critical care physicianis often comes across cases where he suspects poisoning but the agent is unkown. In this article we have focused on the utility of toxidromes which are a constellation of findings, either from the physical examination or from ancillary testing, which may result from any poison in narrowing the radius of suspiscion. There are numerous toxidromes defined in the medical literature. This article focuses on them or ecommon toxidromes described in clinica ltoxicology. Although the set oxidromes canaid the clinician in narrowing the differential diagnosis, care must be exercised to realize the exceptions and limitations associated with each.

Key words : Critical care, toxidrome

Introduction :

Proper diagnosis is the cornerstone for optimal management of poisoned patients. Since the definitive analytical confirmation of the nature of the toxicant involved in the poisoning cannot be rapidly obtained in the majority of healthcare facilities, diagnosis relies on the medical history and the rigorous clinical examination of the patients well as results of the routine biological tests and the electrocardiogram. With the list of possible substances that people overdose on growing every day, it seems a daunting task to stay on top of the game and, as a physician, quickly determine what someone has been exposed to, and anticipate what complications may arise and what treatment will be necessary. The profile of patients with acute poisoning and their choice of agents not only depend upon the socioeconomic, religious and cultural status, but it also greatly varies between different countries. The concept of toxidromes and a little bit of memory work can go a long way towards mastering this task consistently. It helps in early identification of poisonous substances, may also assist in prevention of some of the effects of poison and early initiation of definitive therapy.

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What is a Toxidrome?

The term was coined in 1970 by Mofenson and Greensher[1]. Toxidromes group drugs together according to the signs and symptoms they generally produce in patients, so when you encounter a patient presenting a certain way, you will be able to recognize the toxidrome so you will be able to shorten the list of 'suspect' drugs which the patient may be under the influence of, as well as alert you to possible complications and treatment options.

General principles of diagnostic procedures in poisonings :

1. Specification of the circumstances of poisoning - Taking a though history from the patient or his / her entourage is an essential step in the diagnostic process.
2. Establishment of thorough clinical examination -
   - General examination : Odor from patient's breath, the color of the skin, urine color, sweating.
   - Respiratory Status : Respiratory depression, tachypnea, hyperventilation, saturation.
   - Circulatory Status : Blood pressure, heart rate, electrocardiogram.
   - Body temperature : Hypothermia, hyperthermia.
   - Neurologic examination : Spontaneousmotor activity (calmness or agitation), vascular tone (hypo - or hypertonia), deep tendon reflexes (hypo - or hyperreflexia), cutaneous plantar reflexes (CPR, indifference or presence of a Babinski sign) and size ofpupils (mydriasis ormiosis).

What are the major Toxidromes

- Anticholinergic,
- Cholinergic,
- Sympathomimetic (adrenergic /stimulant),
- Opiod / Narcotic and
- Sedative-hypnotic.
- Hallucinogens

Anticholinergics

Hot as a Hare, Mad as a Hatter, Red as a Beet, Dry as a Bone, Blind as a Bat"[1]

The anticholinergic toxidrome, as the name implies, is a group of drugs that interfere with the binding of acetylcholine to muscarinic receptors.[2] The basic effect of blocking the muscarinic receptors, is to block the parasympathetic nervous system. It commonly follows the ingestion of a wide variety of prescription and over-the-counter medications[3,4,5]. Clinical manifestations are caused by CNS effects, peripheral nervous system effects, or both. Common manifestations are Flushing, Dry skin and mucous membranes, Mydriasis with loss of accommodation, Altered mental status (AMS), Fever. Additional manifestations include Sinus tachycardia, Decreased bowel sounds, Functional ileus, Urinary retention, Hypertension, Tremulousness, Myoclonic jerking.

Sympathomimetics / Withdrawal

Fight or Flight

The sympathomimetic toxidrome mimics the sympathetic nervous system effects. Alcohol and drug withdrawal present the same way as sympathomimetics, which is why they are grouped together. The effects of drugs that mimic the sympathetic nervous system arepredictable : Tachycardia, Dysrhythmias, Hypertension, Diaphoresis, Goosebumps Delusions, Paranoia, Seizures, Increased temperature, Dilated pupils. Patients should be queried about the use of cocaine, methamphetamine, and ecstasy. In addition, patients should be asked about their use of over-the-counter cold medications (containing ephedrine) and herbal preparations (eg, ephedra, Ma-Huang). Looking at the above list, one can appreciate how the sympathomimetic toxidrome could be mistaken for an anticholinergic toxidrome or vice versa. The distinguishing features are diaphoresis and pale skin in sympathomimetics, versus flushed, dry skin in the anticholinergic toxidrome.

Cholinergic / Anticholinesterase

Things Leaking From Every Orifice. Yuk!

As the name implies, this toxidrome leads to elevated levels of acetylcholine, either through direct 'cholinergic' effects or by inhibiting the enzyme responsible for the breakdown of

Table 1 : AnticholinergicToxidrome

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Anticholinergic	Hypervigilance agitation, hallucinations, delirium with mumbling speech, coma	**Mydriasis**	Hyperthermia Tachycardia, Hypertension, Tachypnea	Dry flushed hot skin, dry mucous membranes, decreased bowel sounds, urinary retention, myoclonus, choreoathetosis, picking behaviour seizures (rare)	Antihistamine Tricyclic antidepressants Antiparkinson agents, Antispasmodic Phenothiazine Atropine, Scopolamine, Belladonna alkaloids (Jimson Weed / Dhatura)

Table 2 : Anticholinergic Toxidrome

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Sympathomimetic	Hyperalert, agitation, hallucinations, paranoia	**Mydriasis**	Hyperthermia, Tachycardia, Hypertension, widened pulse pressure, Tachypnea, Hyperpnea	**Diaphoresis,** Tremors, Hyperreflexia, Seizures **Hyperactive bowel sounds** **bronchospasm**	Cocaine, Amphetamines, Ephedrine, Pseudoephedrine Phenylpro--panolamine, Theophylline, Caffeine

acetylcholine (cholinesterase). The symptoms associated with this toxidrome are associated with both nicotinic and muscarinic effects. The effects are outlined in two well known acronyms;

DUMBELS:	**SLUDGE :**
Diaphoresis, Diarrhea, Decreased blood pressure	Salivation
Urination	Lacrimation (Tearing)
Miosis	Urination
Bronchorrhea, Bronchospasm, Bradycardia	Defecation
Emesis, Excitation of skeletal muscle	GI distress
Lacrimation (tearing)	Emesis

Opiate (Narcotic)

The opiates are also called narcotics, from the Greek word narkotikos which means 'to numb'[8] This is a common source of confusion since the term narcotics is often used to refer to all illegal drugs[8]. The Centers for Disease Control and Prevention reports that in 2015, drug overdoses involving an opioid accounted for 33,091 US deaths, a 15.6% increase from 20149.

Opiate toxicity should be suspected when the clinical triad of central nervous system (CNS) depression, respiratory depression, and pupillary miosis are present; respiratory depression is the most specific sign. Opiates bind to opioid receptors in the central nervous system, to produce the following signs and symptoms;

- Pin-point pupils (Miosis);
- Respiratory depression - Due to decreased sensitivity of the respiratory center to CO_2[11].
- This can be very pronounced, even as slow as 2-4 breaths / min!
- Sedation Often GCS 3
- Nausea and vomiting Due to stimulation of the chemoreceptor trigger zone[11].
- Hypothermia - Due to inhibition of the thermoregulatory area[11].

Table 3 : Cholinergic / Anticholinesterase Toxidrome

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Cholinergic	Confusion, Coma	**Miosis**	Bradycardia, hypertension / hypotension, tachypnea / bradypnea	Salivation, urinary and fecal incontinence, diarrhea, emesis, diaphoresis, lacrimation, GI cramps, bronchoconstriction, muscle fasciculations and weakness, seizures	Organophosphates and carbamates, Nerve agents, Nicotine, Pilocarpine, Physostigmine Edrophonium, Bethanechol, Urecholine, muscarinic mushrooms

Sedative-hypnotic

Usually caused by overdose of therapeutic drugs prescribed during course of treatment. Usual symptoms are Coma, respiratory depression, miosis, hypotension, bradycardia, hypothermia, pulmonary edema, decreased bowel sounds, hyporeflexia, needle marks.

Hallucinogens

Hallucinogens comprise a unique collection of substances that are used to induce hallucinations or alterations of consciousness. Hallucinogens are drugs that cause alteration of visual, auditory, or tactile perceptions but are also referred to classes of drugs that cause alteration of thought and emotion.

Patients under the influence of hallucinogenic agents may have a wide range of physical exam findings, depending on the agent but usually present with symptoms enumerated in Table 6.

Summary

The patients who are admitted to ICU may pose an immense diagnostic and therapeutic challenge for the intensivist as a high index of suspicion for intoxication is warranted. The protean manifestations of intoxication challenge even the most astute clinicians, particularly when patients

Table 4 : Opiate (Narcotic) Toxidrome

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Opioid	CNS depression, Coma.	**Miosis**	Hypothermia Bradycardia, Hypotension, apnea/ bradypnea	Hyporeflexia, pulmonary edema, needle marks	Opioids (Morphine, Heroin, Methadone, Oxycodone, Hydromorphone, Diphenoxylate

Table 5 : Sedative-hypnotic Toxidrome

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Sedative-Hypnotic	CNS Depression, confusion, stupor, coma	**Miosis (usual) sometimes mydriasis**	Hypothermia, Bradycardia, Hypotension, apnea/ bradypnea	Hyporeflexia	Benzodiazepines, Barbiturates, Meprobamate Glutethimide Alcohols, Zolpidem

Table 6 : Hallucinogen Toxidrome

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Hallucinogenic	Hallucinations perceptualdistor--tions, depersonalization, Agitation	**Mydriasis (usually)**	**Hyperthermia tachycardia, hypertension, tachypnea**	**Nystagmus**	Phencyclidine LSD, Mescaline, Psilocybin, designer Amphetamines, (MDMA ["Ecstasy"], MDEA)

present with altered mental status or when there is no history of intoxication. The etiologic evaluation in a presumed poisoned patient requires a targeted history and also a thorough physical examination, ECG and, if necessary, routine biological analysis, to find out atoxidrome. Emergency treatment decisions are relied on the initial clinical approach. The onlytoxicologic analysis that is useful to establish diagnostic certainty and prognosis evaluation is measurement of blood concentration of atoxic agent guided by the initial clinical approach based on toxidromes. Meanwhile the toxidromes provide a viable way to proceed with the management of the patient with presumed diagnosis and early initiation of definitive therapy especially in Indian scenario where the toxicological analysis of the blood sample is logistically and economically not always a possibility.

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